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EXAMINER	
STAPLES, MARK	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
04/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/560,236	WINTER ET AL.	
	Examiner	Art Unit	
	MARK STAPLES	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *10 and 13-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 11, 12, and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/16/2009 has been entered.

2. Applicant's amendment of claims 1 and 25 in the paper filed on 11/19/2009 is acknowledged.

Claims 1-9, 11, 12, and 25 are pending and at issue.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

3. Receipt is acknowledged of the paper, which is a certified English translation of German application no. DE 103 26 302.0 with a filing date of June 11, 2003, submitted under 35 U.S.C. 119(a)-(d), which paper has been placed of record in the file.

Rejections that are Withdrawn

Claim Rejections Withdrawn - 35 USC § 112 Second Paragraph

4. The rejection of claims 1-9, 11, and 12 under 35 USC § 112 Second Paragraph is withdrawn. Applicant is advised that the Office currently does not recognize Wikipedia® as an acceptable source of technical information and thus the printouts from Wikepedia® are not persuasive. However, Applicant's argument is persuasive in the part that the terms "pyrimidine nucleotide analog" and a "nucleotide analog" were known in the art. Thus the rejection is withdrawn.

Claim Rejections Withdrawn - 35 USC § 103(a)

5. The rejection of claims 1-9, 11, and 12 under 35 U.S.C. 103(a) as being unpatentable over Tyagi et al. (November 21, 2000), Weisburg et al. (August 29, 2000), and Nunnally et al. (1997) is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendment.

Although the rejection is moot, in regards to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that the Z spacers of the probe do not hybridize to the target sequence) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore the specification does not exclude Z spacers, oligopyrimidine sequences, from hybridizing to the target nucleic acid.

6. The rejection of claim 25 under 35 U.S.C. 103(a) as being unpatentable over Tyagi et al. (United States Patent No. 6,150,097 issued November 21, 2000), Weisburg et al. (United States Patent No. 6,110,678 issued August 29, 2000), and Nunnally et al. (1997) is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendment.

New Rejections Necessitated by Amendment

New Claim Rejections - 35 USC § 112, First Paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7-9, 11, 12, and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The current claims recite a probe, comprising a pyrimidine nucleotide analog or nucleotide analog as set forth in the independent claims 1 and 25 and dependent claim 5. Further the dependent claims 2-4, 7-9, 11, and 12 recite various modifications of other elements of the probes. This large genus of structural variants is represented in the specification by the nucleotide analogs which are PNA or LNA building blocks. Thus, applicant has expressed possession of only two subsets in a genus, which comprises hundreds of millions of different possibilities. The written description guidelines note

regarding such genus/species situations that "Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) Here, no common elements or attributes of the variants of pyrimidine nucleotide analogs as set forth in the independent claims 1 and 25 are disclosed. No common elements or attributes of the variants of nucleotide analogs as set forth in the claim 5 are disclosed. With regard to the various substitutions or modifications of pyrimidine nucleotide analogs and nucleotide analogs with various functional groups, this is insufficient to demonstrate identity of all specific compounds of the claimed invention. Instant claims are overly broad in the recitation of "comprising" since no guidance is provided as to which of the variant compounds would function as nucleotides in probes. Further no information is given in the specification regarding a methodology to determine such common elements or attributes.

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by

describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

It is noted that in *Fiers v. Revel* (25 USPQ2d, 1601), the Fed. Cir. concluded that "when an inventor is unable to envision the detailed chemical structure of the gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred".

In the application at the time of filing, there is no record or description which would demonstrate conception or written description of various compounds of pyrimidine nucleotide analogs or nucleotide analogs comprising modifications of the disclosed pyrimidine nucleotides and disclosed nucleotides and no correlative structure claimed product.

Accordingly, the specification does not provide a written description of the invention of claims 1-5, 7-9, 11, 12, and 25.

New Claim Rejections - 35 USC § 112, Second Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 7 contains the trademark/trade names RHODAMINES™, BODIPY™, and ALEXA™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademarks or trade names cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade names are used to identify/describe fluorescent labeling groups and, accordingly, the identification/description is indefinite. This rejection can be overcome by reciting a unique chemical name along with each respective trademark or otherwise specifically identifying the intended substance, provided there is support in the originally filed application.

New Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-9, 11, 12, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rudert et al. (1997) Tyagi et al. (United States Patent No. 6,150,097 issued 2000, previously cited), Weisburg et al. (United States Patent No. 6,110,678 issued 2000, previously cited), and Nunnally et al. (1997, previously cited).

Regarding claims 1 and 25, Rudert et al. teach probes (entire article) having the general structural formula (I):

5'-M-$(Z)_n$-X_1-X_2-... X_m-$(Z)_n$'-M'-3'

wherein X_1, X_2 ... and X_m are in each case an arbitrary nucleotide or nucleotide analog and in which the sequence X_1- X_2 -... X_m is a probe sequence which is capable of binding to an analyte (see the sequence of the TET-DR control probe and its analyte target which is the Hairpin in Figure 3) and also see the DRB specific probe where m is 18 (see legend to Figure 5) and allowing for Z's as follows

Z is a spacer, in each case independently, pyrimidine nucleotides being thymidine and cytidines of CTTC at the 5' end and thymidine of T at the 3' end,

M and M' are fluorescent labeling groups, where M is a reporter fluorescent dye at the 5' of either 6-FAM, HEX, or TET and M' is the quencher fluorescent TAMRA dye at the 3' end (see the 1st full paragraph of body text on p. 1141 and see the TET-DR control probe in Figure 3),

n and n' are integers respectively of 4 which is within the range of from 1 to 15 and also within the range of 3-10 and of 1 which is within the range of from 1 to 15, and

m is an integer corresponding to the length of the probe sequence and wherein $(Z)_n$ does not hybridize with $(Z)_{n'}$, as neither the TET-DR probe nor the DRB specific probe has complementary ends (see Figures 3 and 5).

Regarding claims 1 and 25, Rudert et al. do not specifically the species election of RHODAMINE GREEN for M and M'. Further regarding claim 25, Rudert et al. teach where n is 4 and thus within the range of 3-10, but do not specifically teach where n' is also within the range of 3-10.

Regarding claims 1 and 25, Tyagi et al. teach that the same fluorescent dye can be used on each of end of probe for a fluorescing and quenching pair (see column 3 lines 45-48). Tyagi et al. teach probes but do not specifically teach where each probe end is a Z which is a pyrimidine nucleotide and wherein $(Z)_n$ does not hybridize with $(Z)_{n'}$. Further regarding claims 1 and 25, Tyagi et al. do not specifically teach the species election of RHODAMINE GREEN for M and M'.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes of Rudert et al. by using the same dye on each end of the probe as suggested by Tyagi et al. with a reasonable expectation of success. The motivation to do so is provided by Tyagi et al. who teach that separation of the same dye as both fluorescing and quenching moieties on ends of a probe alters the absorption spectra in a detectable fashion (see column 3 lines 40-48) and that the separation can be achieved by cleavage of the probe (see column 3 lines 1-32) as also taught by Rudert et al. (see Figure 3 and its legend). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Regarding claims 1, 4, 5, 9, 11, 12, and 25, Weisburg et al. teach probes where Z_n is a repetitious sequence of at least C_5 by teaching C_n, or of at least T_5 by teaching T_n where n is at least about 10 bases (column 8 Lines 36-59). And it is noted that the repetitious sequences of Weisberg et al. do not hybridize with the target sequence but to a synthesized complement which can be on a solid phase (see Figure 4). Weisburg et al. teach that fluorescent moieties well known in the art can be used on probes (column 19 lines 29-34), but do not specifically teach where the fluorescent moiety is RHODAMINE GREEN™ and do not specifically teach the same fluorescent moiety on each end of a probe.

Regarding claim 2, Weisburg et al. teach the further specie election of formula (II) where X is - O-; Y is =O; Y' is -OH; and R is –OH (see Structure 1 in column 13).

Regarding claims 3 and 6, Weisburg et al. teach thymidine 2' deoxynucleotides (see Example 1).

Therefore, regarding claim 25, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probes with pyrimidine ends of Rudert et al. and Tyagi et al. to ends of poly pyrimidines of at least 3 to 10 repetitious pyrimidines as suggested by Weisburg et al. with a reasonable expectation of success. The motivation to do so is provided by Weisburg et al. who teach that probes having repetitious sequences are useful for capturing, separating, and detecting a target polynucleotide and which can be employed in diagnostic procedures (see column 1 lines 11-17) . Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Regarding claims 1, 4, 7- 9, and 12 Nunnally et al. teach fluorescein, as also taught by Tyagi et al. above, and that RHODAMINE GREEN™ may be substituted for fluorescein (see Table 1 and see the 1st full paragraph in the 2nd column on p. 2394). Nunnally et al. teach that the use of fluorescein in probes was well known (see 1st full paragraph on p. 2392).

Rudert et al. in combination with Tyagi et al. teach pyrimidine nucleotides on the ends of a probe and teach identical fluorophores including fluorescein on the ends of the claimed probes. Weisburg et al. teach multiple pyrimidine nucleotides on the ends

of probes and fluorescent labels on the ends of these. Nunnally et al. teach that the use of fluorescein was well known and that RHODAMINE GREEN™ may be substituted for fluorescein. Because Rudert et al., Tyagi et al., and Weisburg et al. each teach well known fluorophores, it would have been obvious to one skilled in the art to substitute the well known fluorescein of Tyagi et al. as the fluorophore for the well known fluorophores of Weisberg to arrive at the claimed probe, but with fluorescein being the identical fluorophore on each end (instead of RHODAMINE GREEN™). As Nunnally et al. teach RHODAMINE GREEN™ may be substituted for fluorescein, it would have been obvious to one skilled in the art to substitute RHODAMINE GREEN™ for the fluorescein of Tyagi et al. and Weisberg et al. in the probe of Rudert et al., Tyagi et al., and Weisburg et al. in order to achieve the predictable result of a probe having ends of pyrimidine nucleotide sequences with RHODAMINE GREEN™ at the ends of each of the pyrimidine nucleotide sequences.

Conclusion

12. No claim is free of the prior art.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark Staples/
Examiner, Art Unit 1637
March 28, 2009